Effect of altered gravity environments on aerosol deposition in the human lung

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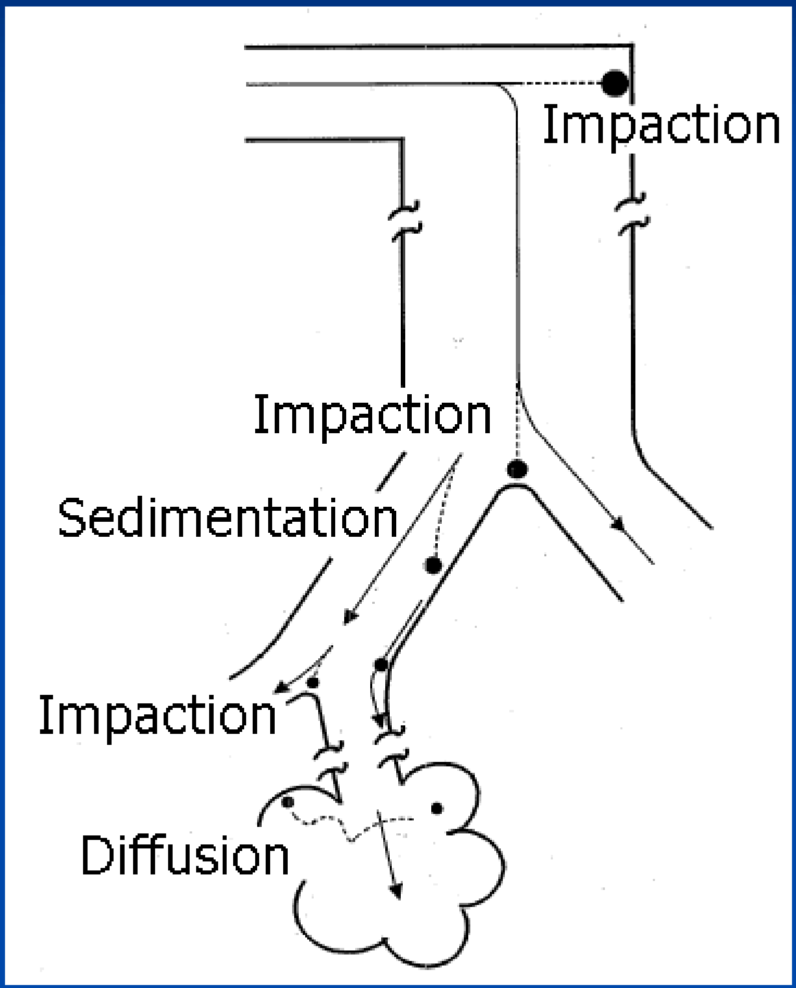
Aerosol = gas + particles



Deposition mechanisms:

- Impaction: >5 _m
- Sedimentation: 1-8 _m
- Diffusion: <1 _m

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Why aerosols are important?

- Atmospheric pollutants
  - Health risk _{ Respiratory
    Cardiovascula
  - EPA standards for $PM_{2.5}$

- Pharmaceutical applications
  - Aerosol drug therapy
  - Drug targeting _{ Increases efficiency
    Decreases side effects

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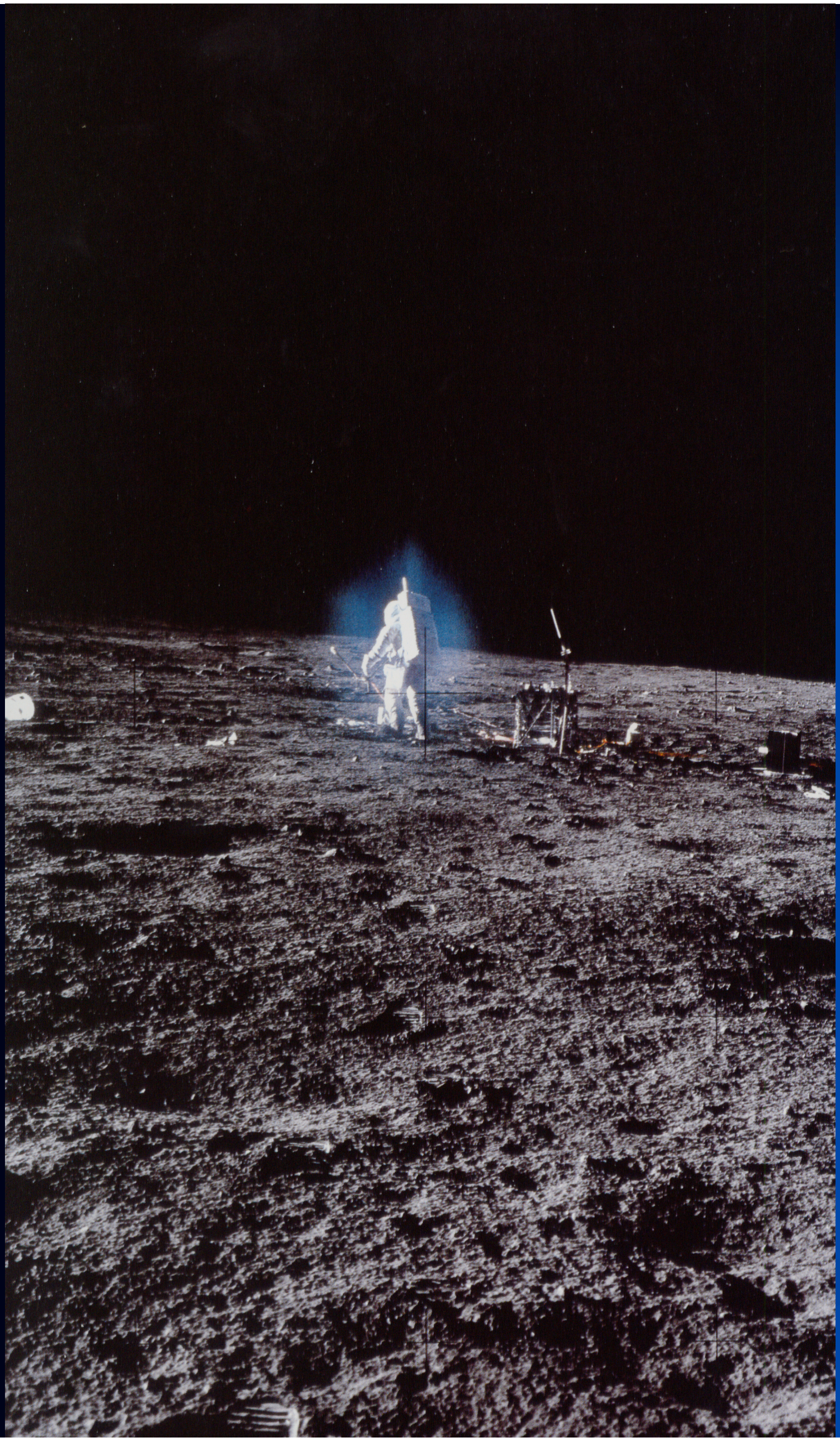
Studies in altered gravity

- Applications on Earth:
  - effect of sedimentation on overall deposition
  - better understanding of site and magnitude of lung deposition _ airborne pollutants

    drug therapy
- Applications in space:
  - no sedimentation _ long term health risk to astronauts ?



Dust halo around astronaut Ed Mitchell (Apollo 14)

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Astronaut Dave Scott (Apollo 15)

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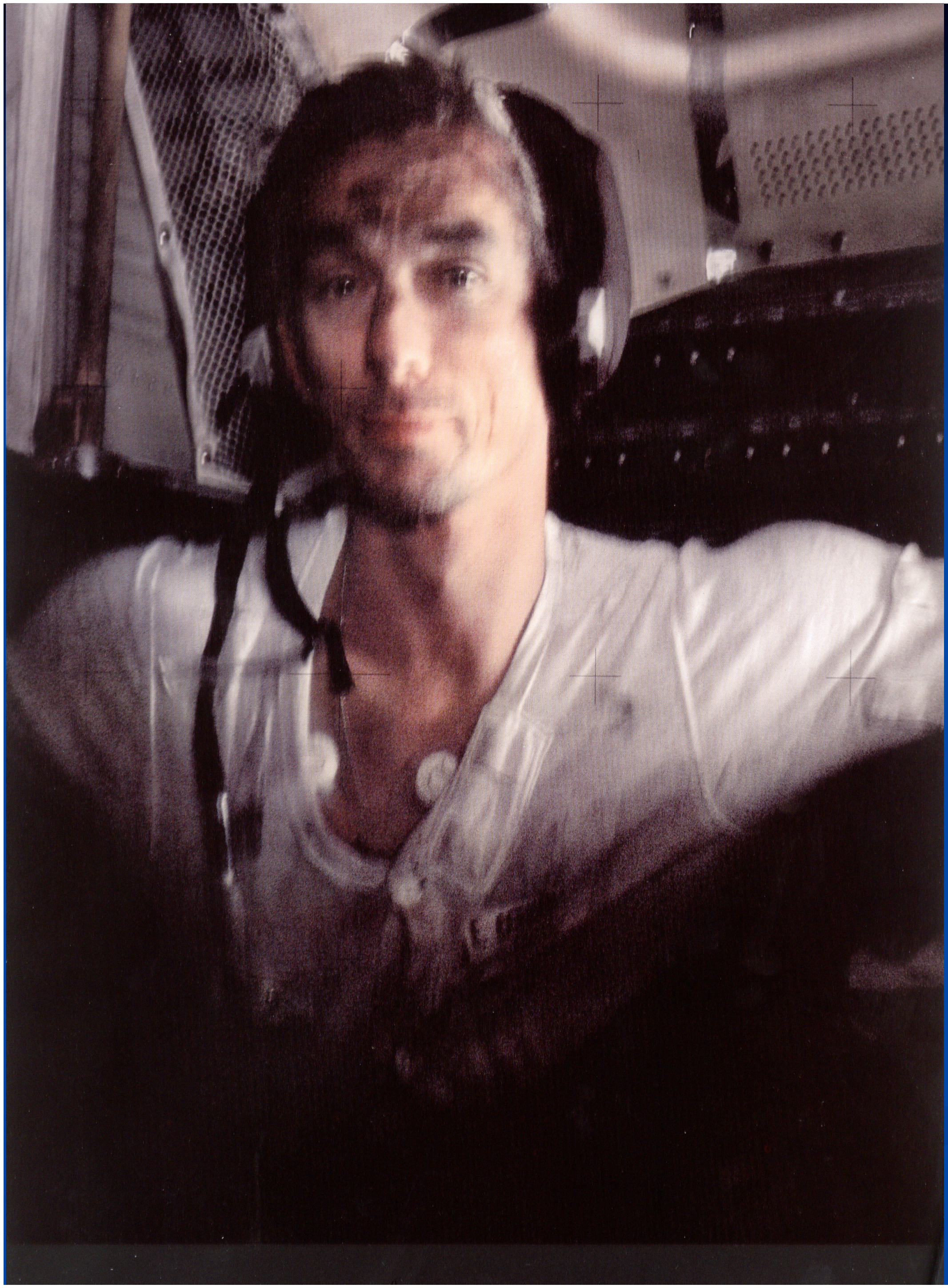

Astronaut Eugene Cernan (Apollo 17, Dec 1972)

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MATURITY INDEX:
I_s/FeO = 66 (mature)

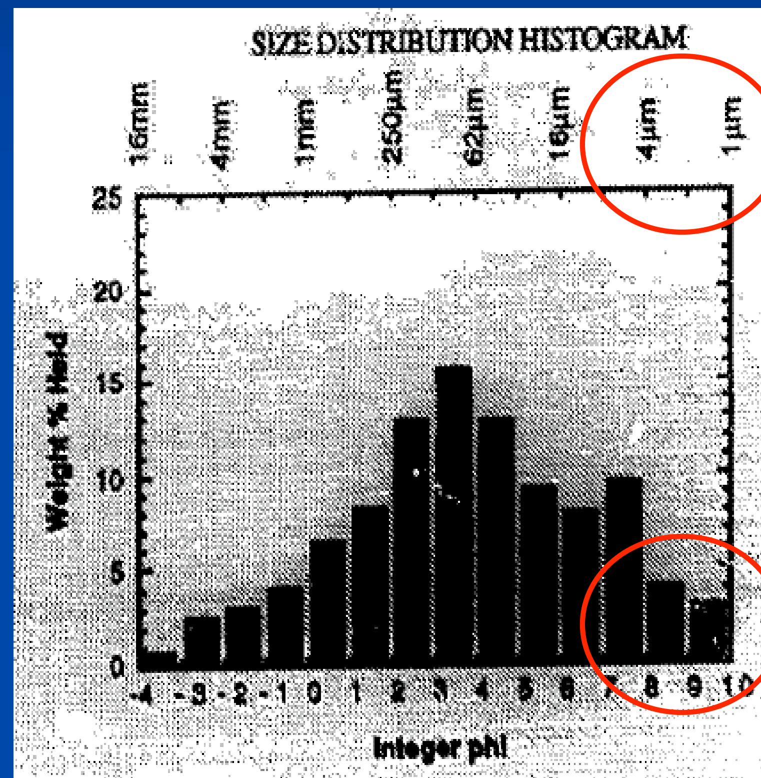
TABULATED SIEVE DATA

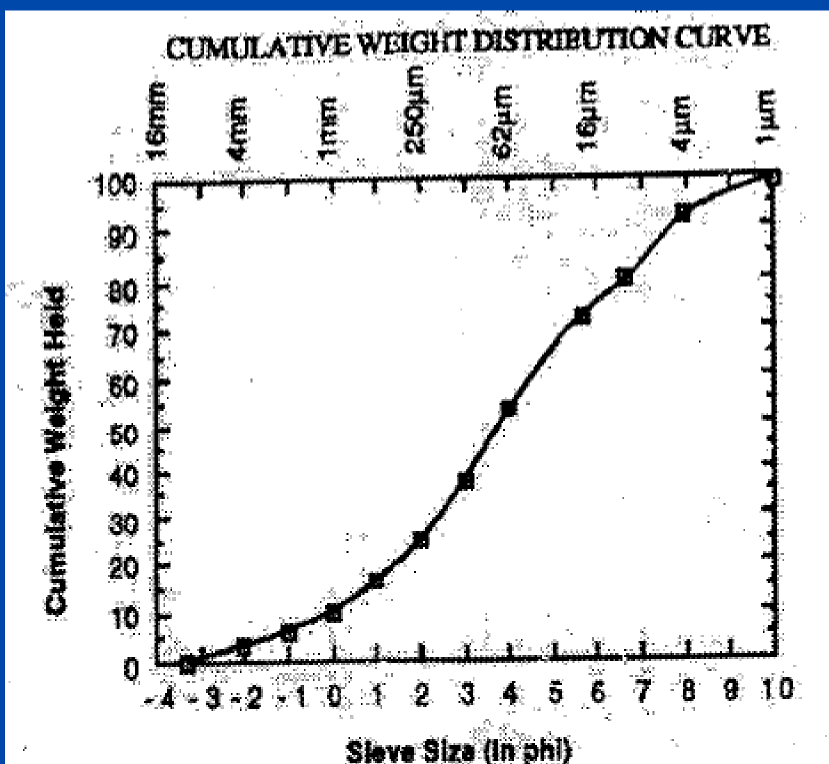
Sieve Size (µm)	Wt %
10000	0
4000	3.1
2000	2.99
1000	3.95
500	6.41
250	8.19
125	12.73
63	15.32
20	19.41
10	7.39
4	12.47
1	7.03

Soil: 14003
(subsample 14003,39)
W.V. Engelhardt PI

Lunar dust

LOCATION COMMENTS:
This contingency sample was collected NW of the LM 100 meters from North Triplet crater. The sample area is level and free of large blocks.





(From NASA-RP-1265: Lunar soil size catalog)

Dust from Mars

- High composition of mineral oxide (SiO_2, FeO)
- Free oxygen radicals that may prove to be highly toxic when brought into contact with the lining of the lung

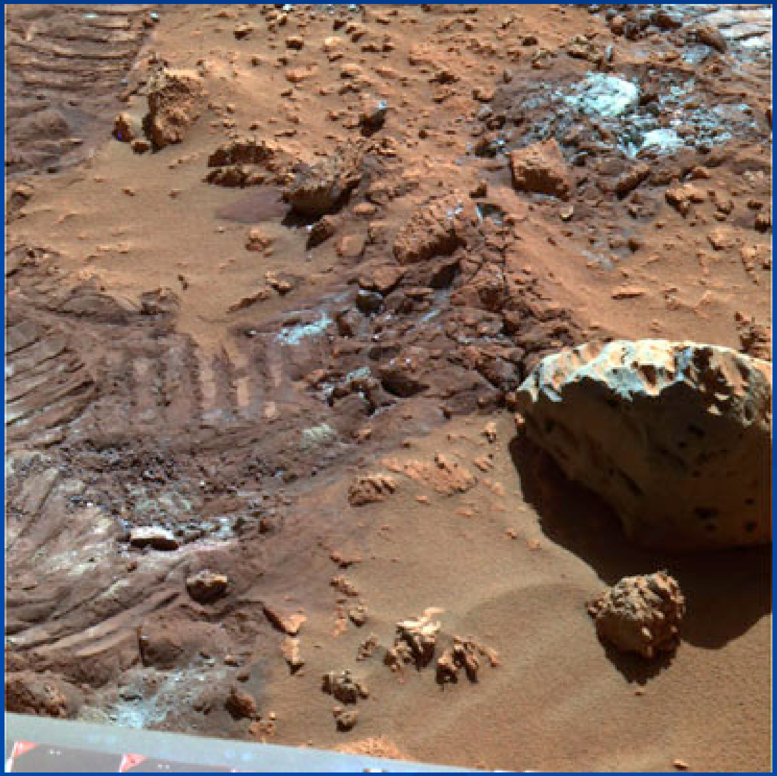


Image credit: JPL/NASA/Cornell

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Potential hazards

- Saline tracheal instillation of simulated lunar and Martian dust in mice showed
  - after 7 days:
    - focal regions of particulate-laden macrophages
    - alveolar, peribronchiolar and perivascular inflammation
  - after 90 days:
    - chronic pulmonary inflammation
    - alveolar septal thickening
    - Fibrosis

(Lam et al., Inhalation Toxicology, 2002)

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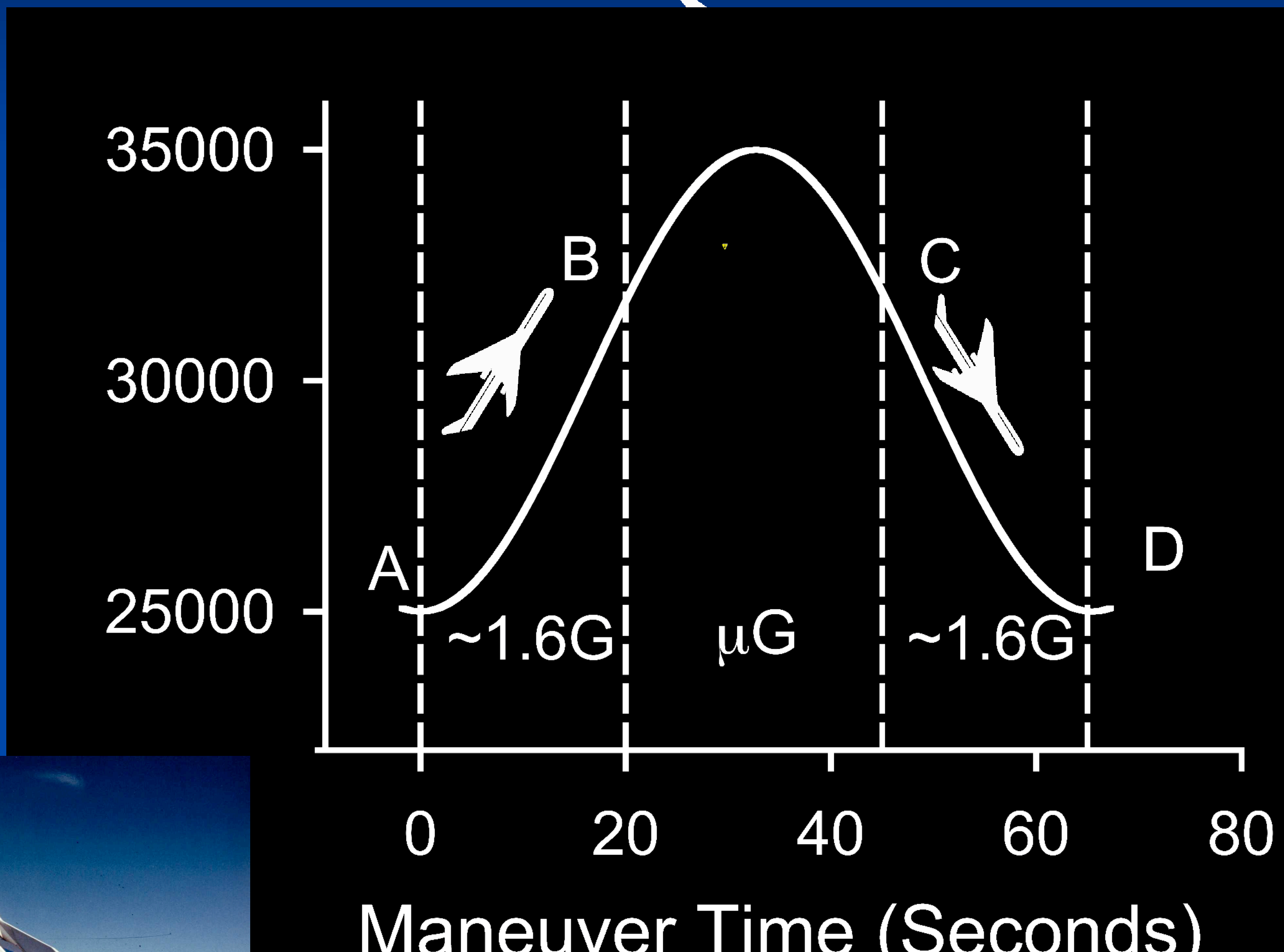
Human Studies

How? Parabolic flights



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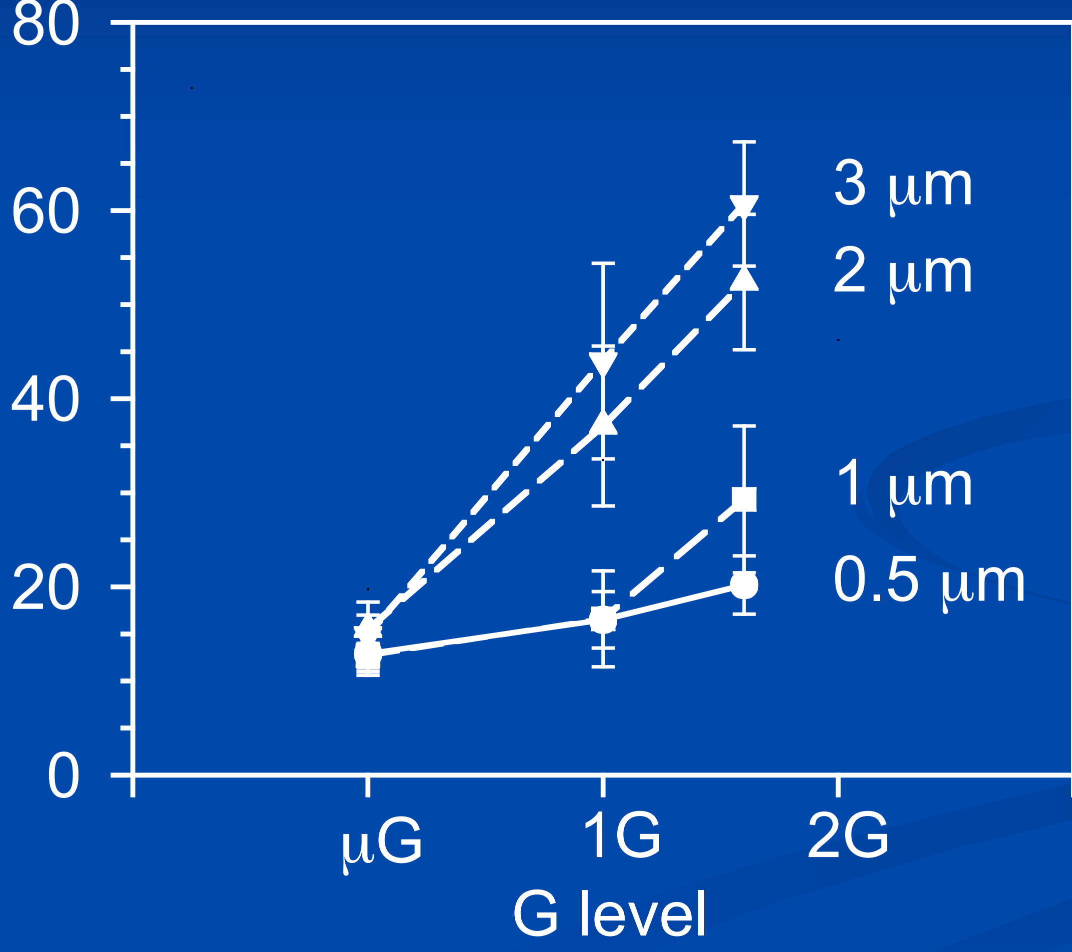
Total deposition depends on both gravity and particle size



(Darquenne et al., *J. Appl. Physiol.*, 1997)

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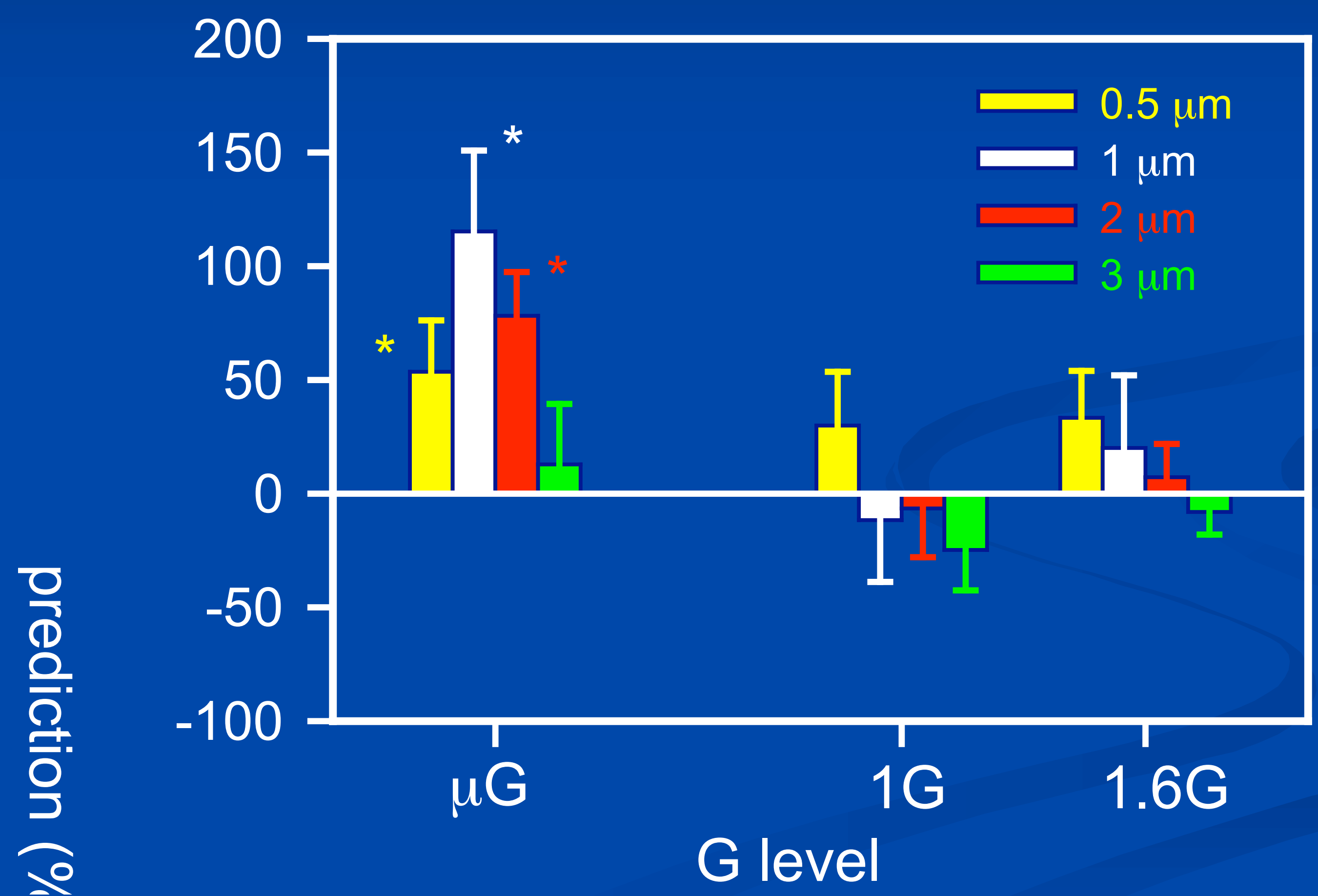
Total deposition of small particles in μG is higher than expected



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Deposition is reduced in _G compared to normal gravity however…

- Reduction in sedimentation results in higher airway concentration
- More particles penetrate deep in the lung
- More particles may deposit in the sensitive alveolar region of the lung

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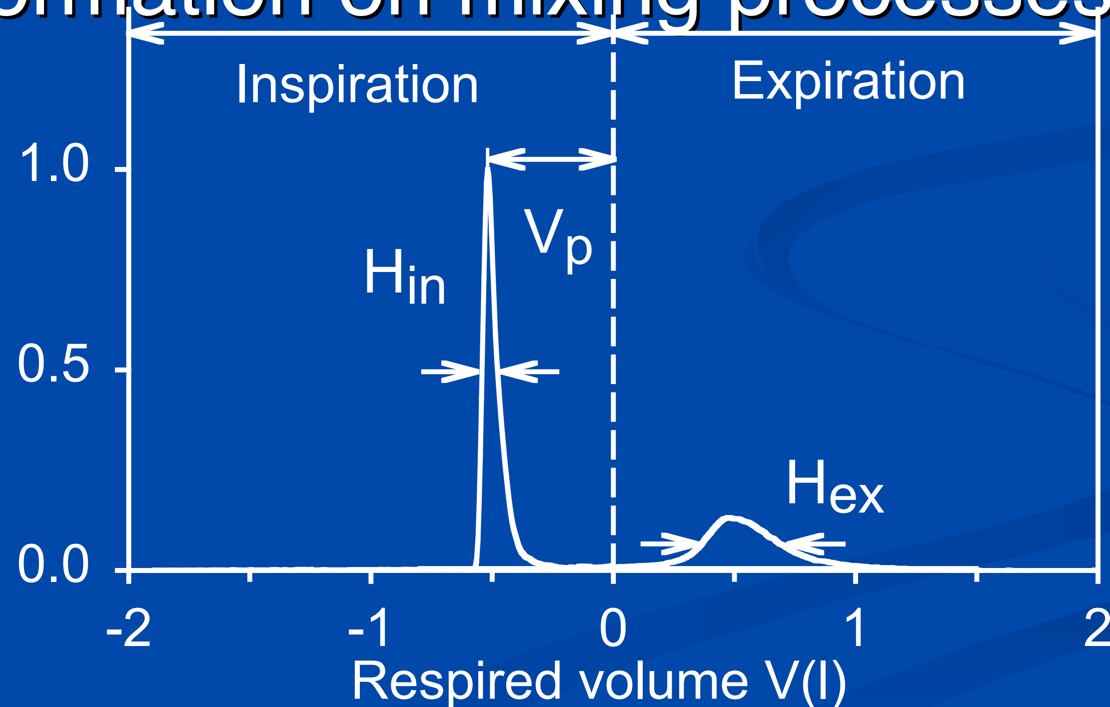
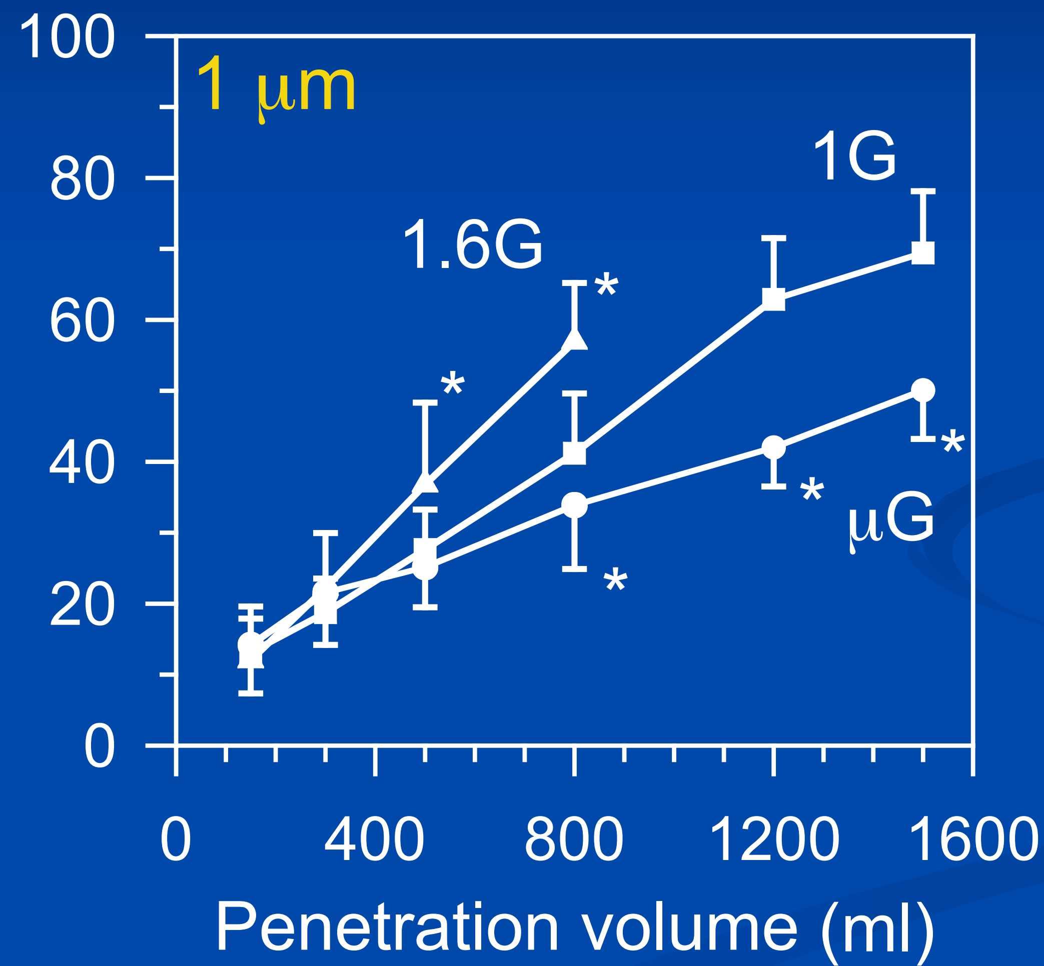
Aerosol bolus test

- Allows probing of different depths of the lung
  - Information on regional deposition
  - Information on mixing processes



Aerosol bolus deposition is affected by gravity



* Significantly different from 1G ($p<0.05$)

(Darquenne et al., *J. Appl. Physiol., 1998)*

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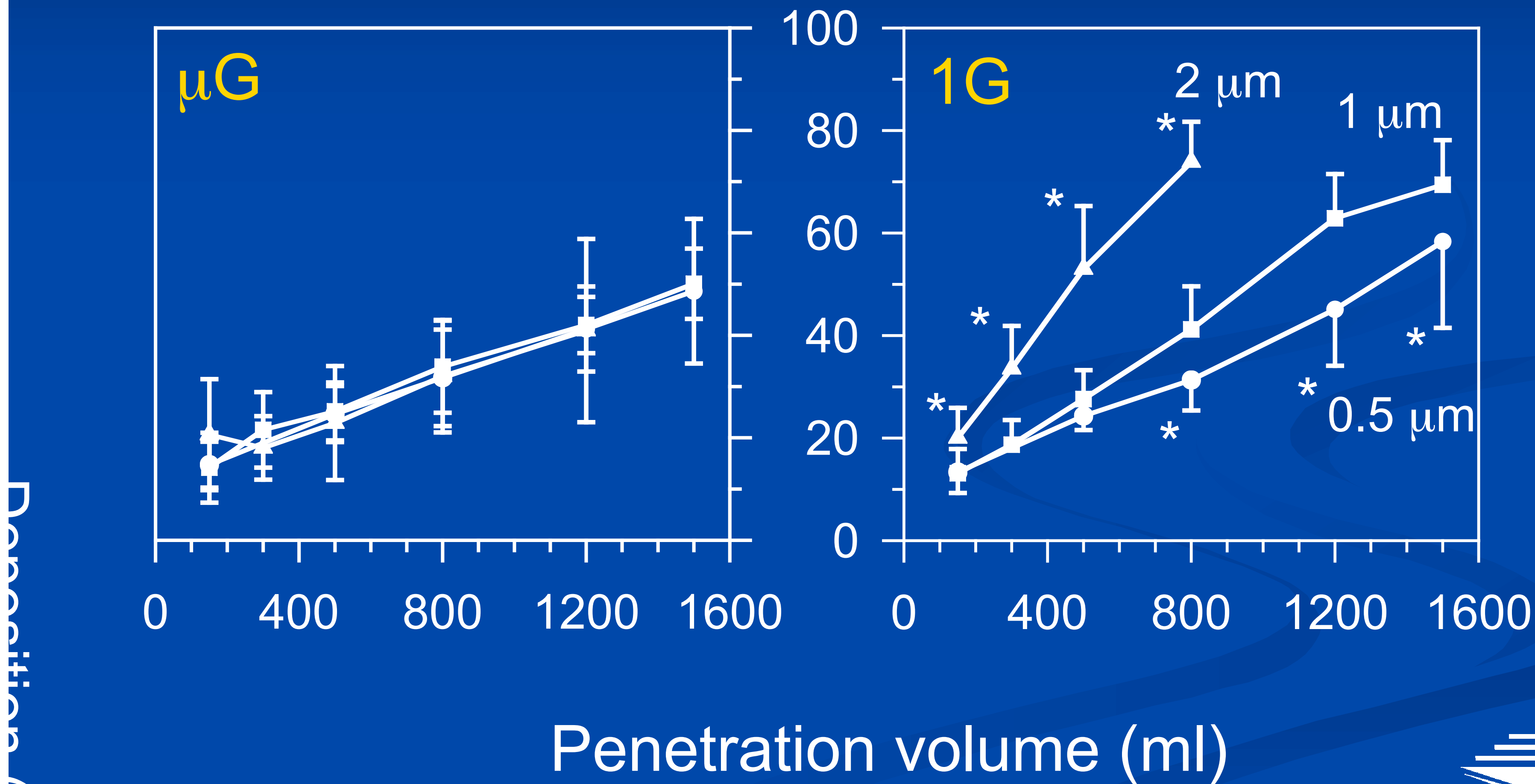
Differences in deposition between particle sizes are solely a function of gravity



(Darquenne et al., *J. Appl. Physiol., 1999)*

Particle mixing in the lung periphery is much more complex than originally thought

Effect of convective stretching and folding on aerosol mixing deep in the lung, assessed by approximate entropy

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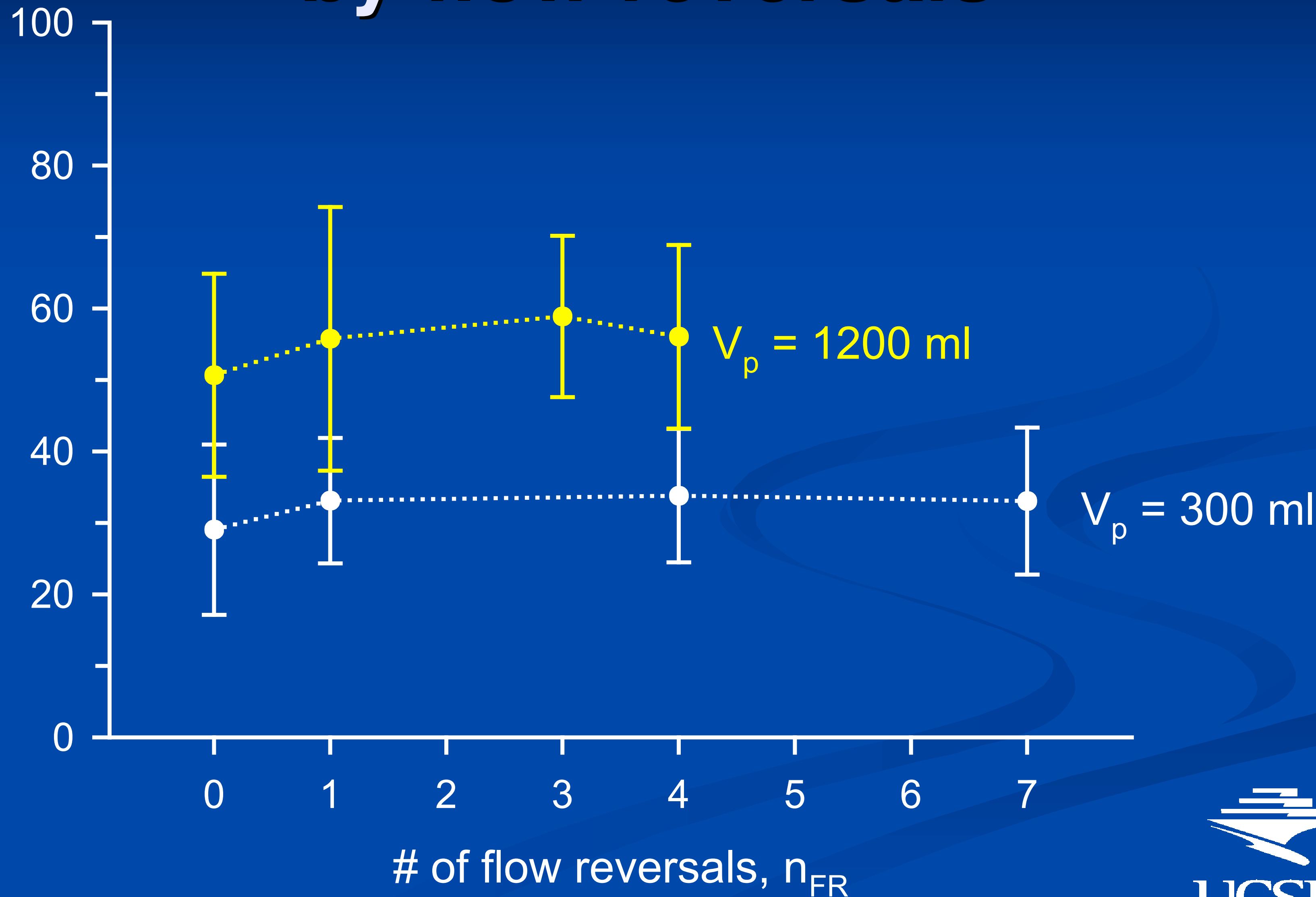
Butler, J. P., and A. Tsuda. Effect of convective stretching and folding on aerosol mixing deep in the lung, assessed by approximate entropy. *J. Appl. Physiol.* 83(3): 800–809, 1997.—There is a surprisingly substantial amount of aerosol mixing and deposition deep in the lung, which cannot be explained by classic transport mechanisms such as streamline crossing, inertial impaction, or gravitational sedimentation with reversible acinar flow. Mixing associated with "stretch and fold" convective flow patterns can, however, be a potent source of transport. We show such patterns in experimental preparations using rat lungs and in the theoretical Baker Transform. In both cases, mixing is associated with the temporal evolution of two length scales. The first is the slowly increasing diffusive length scale. The second is the rapidly decreasing lateral length scale, due to "stretching and folding," over which diffusion must take place. This interaction leads to aerosol mixing in much shorter times than previously appreciated. Finally, we propose a new method by which to quantify the state of mixing, using an approximation to the entropy of the aerosol concentration distribution. The results of the analysis suggest that stretching and folding may be a key feature underlying peripheral aerosol transport.

aerosol deposition; convection; diffusion; chaos; chaotic mixing; acinar flow

erto appreciated. The stretch and fold pattern of convection is qualitatively much different from laminar or even turbulent steady flow in tubes, but it is easily visualized. It is evident in common everyday occurrences: mixing of different colors of paint in a can, cream in coffee, and mixing of cinnamon and sugar in a bowl. These all display the striking feature that, over a certain number of cycles, there is an increasingly detailed fine structure in the pattern, which is followed by a threshold number of cycles where the mixing characteristics qualitatively change from one with a fine but well-defined structure to one which is, in effect, completely mixed. This phenomenon is characteristic of the stretch and fold convective kinematics. During such repeated stretching and folding, two important convective characteristics emerge. First, the area over which diffusion can take place grows exponentially in time or cycle number and, second, the lateral or transverse distance scales from one fold to its neighbor decrease exponentially in time or cycle number. These two features together imply that the classic theories [e.g., for steady laminar pipe flow (2, 11) and cyclic flow (15)] are inadequate to explain the interaction of convection

Deposition is not affected by flow reversals



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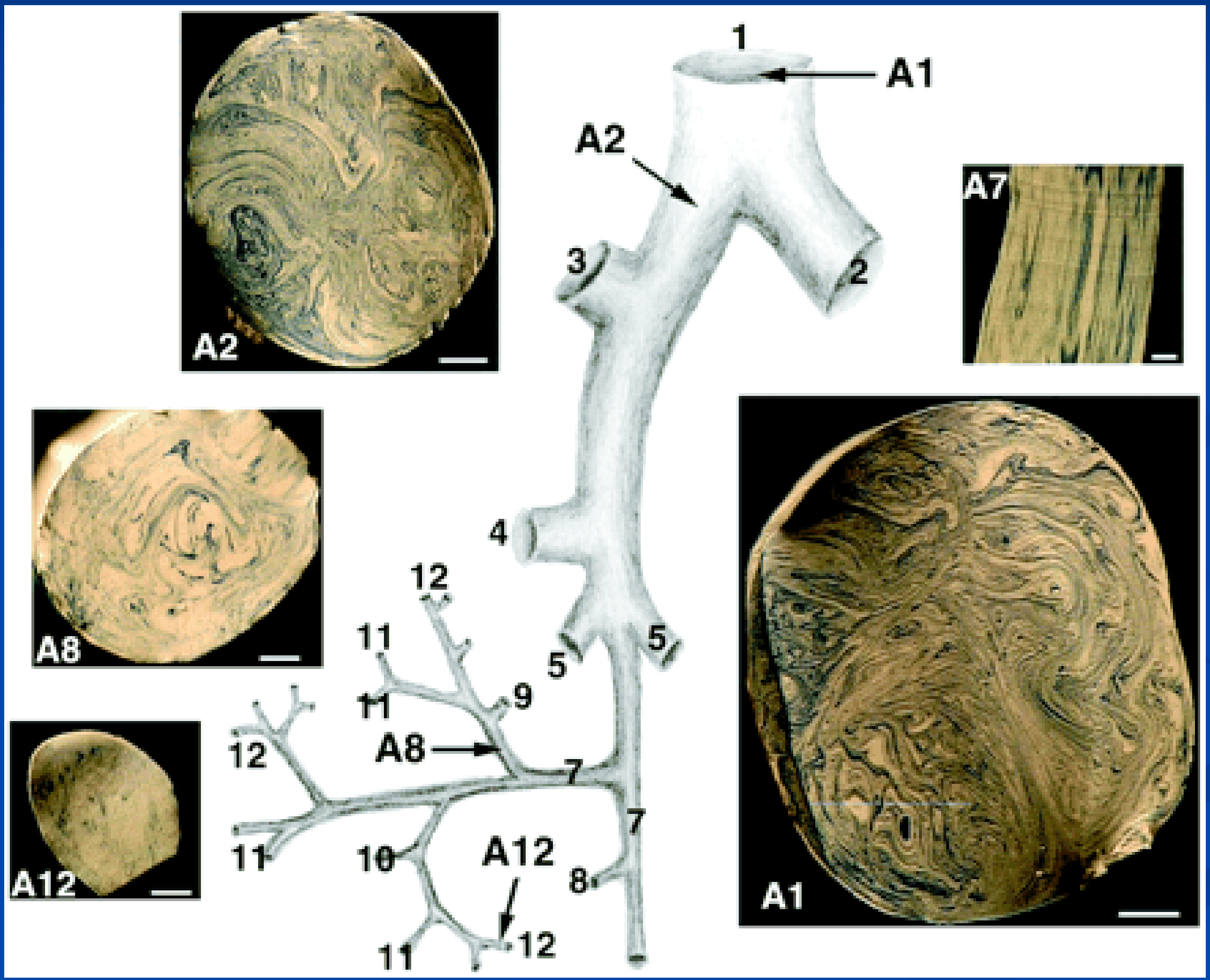
Increasing number of flow reversals has no effect on aerosol deposition

- The mechanism of stretch and fold likely occurs in one breathing cycle

Typical flow patterns in the rat lung after one breathing cycle



(From Tsuda et al., *Proc. Nat. Acad. Sci.*, 2002)

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Increasing number of flow reversals has no effect on aerosol deposition

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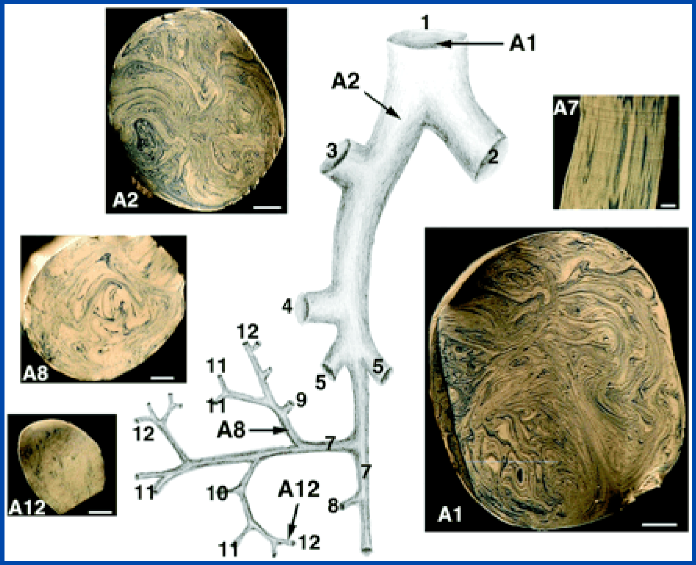

- It provides a mechanistic basis to explain what we previously described as "enhanced diffusion resulting from unaccounted mixing mechamisms" in the total deposition studies

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Proposed Rat Studies

- Short-term objective: develop a rat model to assess deposition patterns in the lung
- Long-term objective: use the rat model to directly assess lung damage caused by inhaled particulates

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Hypothesis

Aerosol deposition in the lungs of spontaneously breathing rats in fractional-G corresponding to the surface of the Moon and Mars will be more peripheral (closer to the alveoli) than in 1G increasing the potential for oxidative lung damage

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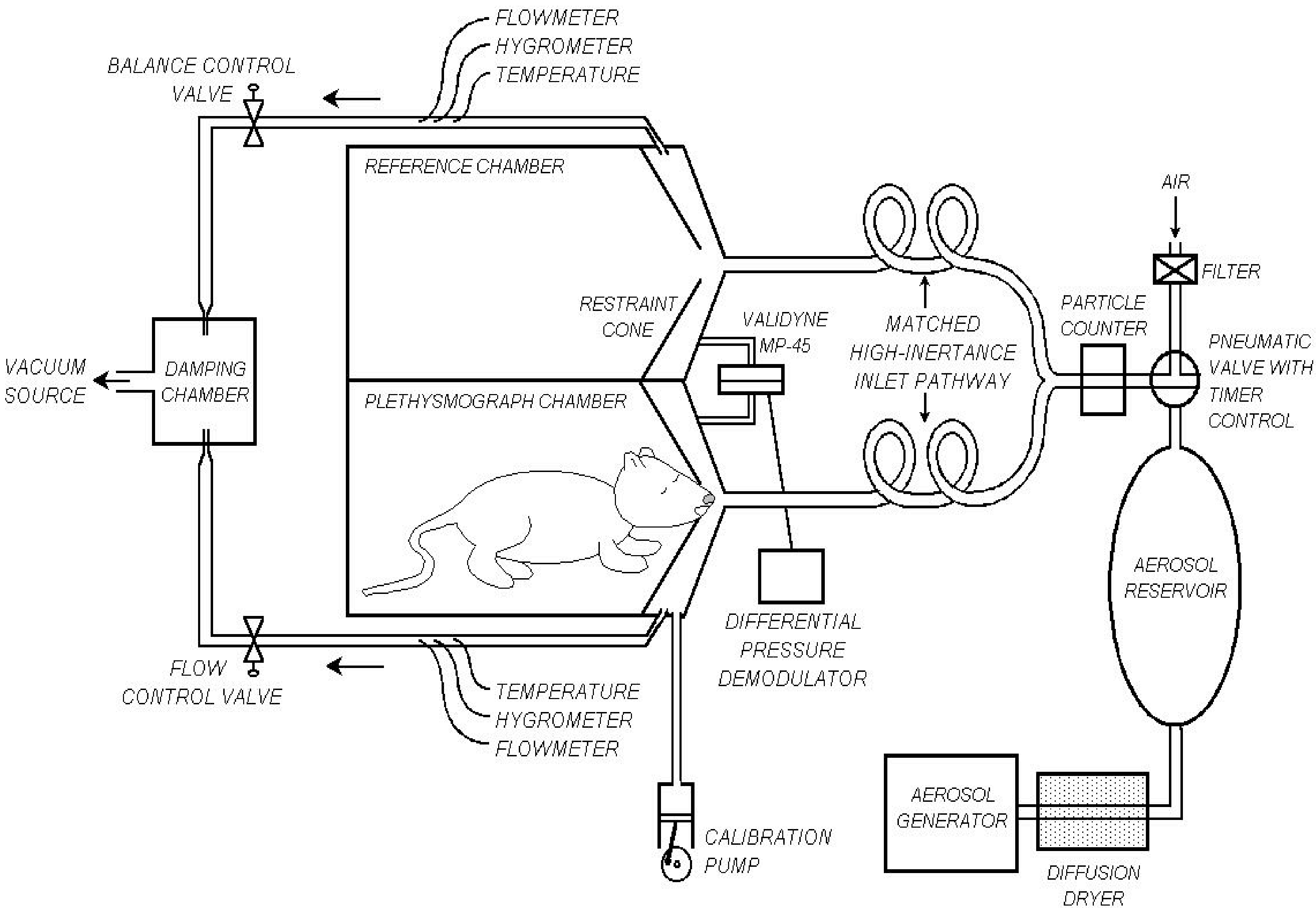
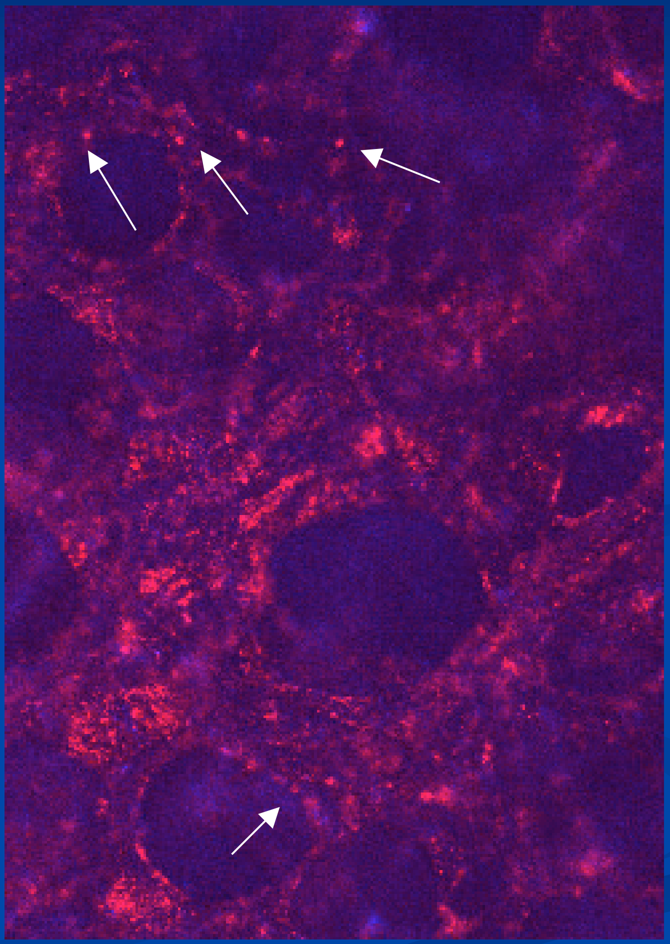


FLOWMETER
HYGROMETER
TEMPERATURE
BALANCE CONTROL VALVE
REFERENCE CHAMBER
AIR
FILTER
RESTRAINT CONE
VALIDYNE MP-45
MATCHED HIGH-INERTANCE INLET PATHWAY
PARTICLE COUNTER
PNEUMATIC VALVE WITH TIMER CONTROL
VACUUM SOURCE
DAMPING CHAMBER
PLETHYSMOGRAPH CHAMBER
AEROSOL RESERVOIR
DIFFERENTIAL PRESSURE DEMODULATOR
FLOW CONTROL VALVE
TEMPERATURE
HYGROMETER
FLOWMETER
CALIBRATION PUMP
AEROSOL GENERATOR
DIFFUSION DRYER

Methods

- Expose rats to fluorescents particles in 1G and fractional G and measure central and peripheral deposition in the lungs using confocal microscopy of lung s



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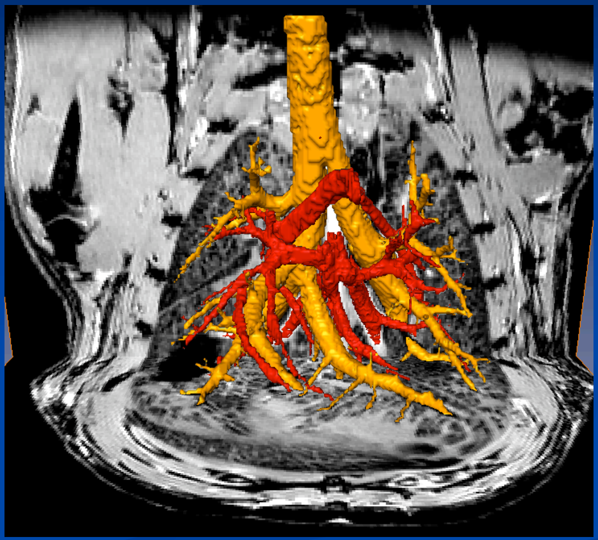
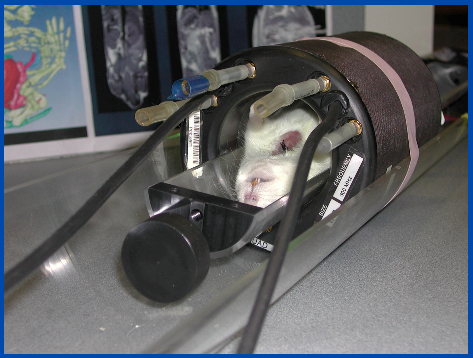
Methods

- Expose rats to MRI-labeled particles in 1G and fractional G and use 3D MRI to measure central and peripheral deposition in the lungs of intact animals





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